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62021 INTAKE/BI

11712 FOOD INTAKE/BI

((FOOD(W)INTAKE)/BI)

112703 FOOD/AB

57680 INTAKE/AB

10915 FOOD INTAKE/AB

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3 L2 AND (REDUC####(2A) FOOD INTAKE)/BI,AB

=> d 1-3 bib, ab

L3

L3 ANSWER 1 OF 3 CA COPYRIGHT 2000 ACS

AN 133:276732 CA

TI Central exendin-4 infusion reduces body weight without altering plasma leptin in (fa/fa) Zucker rats

AU Al-Barazanji, Kamal A.; Arch, Jonathan R. S.; Buckingham, Robin E.; Tadayyon, Mohammad

CS Department of Vascular Biology, SmithKline Beecham Pharmaceuticals, Essex,

UK

SO Obes. Res. (2000), 8(4), 317-323 CODEN: OBREFR; ISSN: 1071-7323

PB North American Association for the Study of Obesity

DT Journal

LA English

AB Aim: To investigate whether chronic administration of the long-acting glucagon-like peptide-1 receptor agonist exendin-4 can elicit sustained redns. in food intake and body wt. and whether its actions require an intact leptin system. Male lean and obese Zucker (fa/fa) rats were

infused intracerebroventricularly with exendin-4 using osmotic minipumps for 8 days. Exe n-4 reduced body wt. in both 1 and obese Zucker rats, max. suppression being reached on Day 5 in obese (8%) and Day 7 in lean (16%) rats. However, epididymal white adipose tissue wt. was not reduced, and only in lean rats was there a redn. in plasma leptin concn. Food intake was maximally suppressed (by 81%) on Day 3 in obese rats but was reduced by only 18% on Day 8. Similarly, in lean rats food intake was maximally reduced (by 93%) on Day 4 of treatment and by 45% on Day 8. Brown adipose tissue temp. was reduced from Days 2 to 4. Plasma corticosterone was elevated by 76% in lean but by only 28% in obese rats. Chronic exendin-4 treatment reduced body wt. in both obese and lean Zucker rats by reducing food intake: metabolic rate was apparently suppressed. These effects did not require an intact leptin system. Neither does the absence of an intact leptin system sensitize animals to exendin-4. Partial tolerance

the anorectic effect of exendin-4 in lean rats may have been due to elevated plasma corticosterone and depressed plasma leptin levels, but other counter-regulatory mechanisms seem to play a role in obese Zucker rats.

RE.CNT 35

RE

to

- (1) Arch, J; Am J Clin Nutr 1981, V34, P2763 CA
- (2) Arch, J; Life Sci 1982, V30, P1817 CA
- (3) Arch, J; Obesity and Cachexia 1991, P241 CA
- (4) Arvaniti, K; Endocrinology 1998, V139, P4000 CA
- (5) Davis, H; Obes Res 1998, V6, P147 CA
- ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L3 ANSWER 2 OF 3 CA COPYRIGHT 2000 ACS
- AN 130:163426 CA
- TI Repeated intracerebroventricular administration of glucagon-like peptide-1-(7-36) amide or exendin-(9-39) alters body weight in the rat
- AU Meeran, Karim; O'Shea, Donal; Mark, C.; Edwards, B.; Turton, Mandy D.; Heath, Melanie M.; Gunn, Irene; Abusnana, Salahedeen; Rossi, Michela; Small, Caroline J.; Goldstone, Anthony P.; Taylor, Gillian M.; Sunter, David; Steere, Joanna; Choi, Sang Jeon; Ghatei, Mohammad A.; Bloom, Stephen R.
- CS Imperial College School of Medicine Endocrine Unit, Hammersmith Hospital, London, W12 ONN, UK
- SO Endocrinology (1999), 140(1), 244-250 CODEN: ENDOAO; ISSN: 0013-7227
- PB Endocrine Society
- DT Journal
- LA English
- Central nervous system glucagon-like peptide-1-(7-36) amide (GLP-1) administration has been reported to acutely reduce food intake in the rat. We here report that repeated intracerebroventricular (icv) injection of GLP-1 or the GLP-1 receptor antagonist, exendin-(9-39), affects food intake and body wt. Daily icv injection of 3 nmol GLP-1 to schedule-fed rats for 6 days caused a redn. in food intake and a decrease in body wt. of 16 q (compared with saline-injected controls). Daily icv administration of 30 nmol exendin-(9-39) to schedule-fed rats for 3 days caused an increase in food intake and increased body wt. by 7 g (compared with saline-injected controls). Twice daily icv injections of 30 nmol exendin-(9-39) with 2.4 nmol neuropeptide Y to ad libitum- fed rats for 8 days increased food intake and increased body wt. by 28 g compared with 14 g in neuropeptide Y-injected controls. There was no evidence of tachyphylaxis in response to icv GLP-1 or exendin-(9-39). GLP-1 may thus be involved in the regulation of body wt. in the rat.

RE.CNT 57

RF.

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- (2) Campfield, L; Science 1995, V269, P546 CA

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(5) Deutsch, J; Natur 977, V266, P196 CA(6) Donahey, J; Brain Res 1998, V779, P75 CA
         ALL CITATIONS AVAILABLE IN THE RE FORMAT
              ANSWER 3 OF 3 CA COPYRIGHT 2000 ACS
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              .129:149256 CA
         ΑN
              Preparation of exendin peptides for the reduction of
         TI^{-}
              food intake
              Beeley, Nigel Robert Arnold; Prickett, Kathryn S.; Bhavsar, Sunil
              Amylin Pharmaceuticals, Inc., USA
         PA
              PCT Int. Appl., 214 pp.
         SO
              CODEN: PIXXD2
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         FAN.CNT 1
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    WO 1998-US449
    WO 1998-US16387 19980806
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    Methods for treating conditions or disorders which can be alleviated by
AB
     reducing food intake are disclosed which
    comprise administration of an effective amt. of an exendin or an exendin
     agonist, alone or in conjunction with other compds. or compns. that
effect
     satiety. Approx. 180 exendin-related peptides were synthesized by the
     solid-phase method.
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L5 8 L4 AND (REDUC#### (2A) FOOD INTAKE)

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L5 ANSWER 1 OF 8 MEDLINE

AN 2000333687 MEDLINE

DN 20333687

TI Peripheral versus central effects of glucagon-like peptide-1 receptor agonists on satiety and body weight loss in Zucker obese rats.

AU Rodriquez de Fonseca F; Navarro M; Alvarez E; Roncero I; Chowen J A; Maestre O; Gomez R; Munoz R M; Eng J; Blazquez E

CS Department of Psychobiology, Faculty of Psychology, Complutense University, Madrid, Spain.

SO METABOLISM: CLINICAL AND EXPERIMENTAL, (2000 Jun) 49 (6) 709-17. Journal code: MUM. ISSN: 0026-0495.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200009

EW 20000904

The present study explores the potential utility of peripheral versus central administration of glucagon-like peptide-1 (GLP-1) receptor agonists in the regulation of feeding behavior in Wistar and Zucker obese rats. Acute central (intracerebroventricular [i.c.v.]) and peripheral (subcutaneous [s.c.]) administration of both GLP-1 (7-36) amide and exendin-4 resulted in a reduction in food intake for at least 4 hours, exendin-4 being much more potent than GLP-1 (7-36) amide, especially after peripheral administration. Both Zucker obese rats (fa/fa) and their lean littermates (Fa/-) responded to acute central and peripheral administration of exendin-4. Moreover, in situ hybridization revealed specific labeling for the mRNA for GLP-1 receptors in several brain areas of both the obese and lean rats. The presence of this receptor was also detected by affinity cross-linking assays. Long-term s.c. administration of exendin-4 (1 single injection

day, I hour prior to the onset of the dark phase of the cycle) decreased daily food intake and practically blocked weight gain in obese rats. In contrast to previous studies, these findings show that peripheral (s.c.) administration of both GLP-1 receptor agonists also induces satiety and weight loss in rats, and suggest the potential usefulness of exendin-4 as

a therapeutic tool for the treatment of diabetes and/or obesity.

L5 ANSWER 2 OF 8 MEDLINE

AN 2000289086 MEDLINE

DN 20289086

TI Exendin-4 decelerates food intake, weight gain, and fat deposition in Zucker rats.

AU Szayna M; Doyle M E; Betkey J A; Holloway H W; Spencer R G; Greig N H; Egan J M

CS NMR Unit, Gerontology Research Center, National Institute on Aging, National Institutes of Health, Baltimore, Maryland 21224, USA.

SO ENDOCRINOLOGY, (2000 Jun) 141 (6) 1936-41.

Journal code: EGZ ISSN: 0013-7227. CY United States Journal; Article; (JOURNAL ARTICLE) DTLΑ English Abridged Index Medicus Journals; Priority Journals; Cancer Journals FS EM 200008 EW 20000803 Exendin-4 is a 39 amino acid peptide produced in the salivary gland of AΒ Gila monster lizard. It has a 53% amino acid homology to the incretin hormone glucagon-like peptide-1 (GLP-1). Exendin-4 induces insulin through activation of the GLP- 1 receptor but is a much more potent insulinotropic agent than GLP-1. Of critical importance for its potential use as a treatment for diabetes is its much longer biological effect in vivo. Previous studies involving once daily administration of exendin-4 over 13 weeks to db/db mice demonstrated that it lowers hemoglobin Alc (HbA1c), a marker of mean blood glucose levels. Food consumption in the treated animals dropped over the first 4 days and then increased to a level comparable with that of the untreated animals. In this study, we initially examined the effect of once daily injections (over 14 days) on the food consumption of Zucker fatty rats. We observed an immediate reduction in food intake which then leveled off(after 5 days) to match that of the untreated animals. Subsequently we injected the same animals twice daily (treatment period of 56 days in total) and observed a sustained reduction in food intake and weight-gain. This was matched by a reduction in the critical parameters of HbAlc, fasting blood glucose and plasma insulin. MRI imaging of the abdominal regions of the animals showed that initially only the amount of fat deposited in the sc region was reduced after 4 weeks exendin-4 treatment. At the 8-week time point there was a corresponding decrease in the amount of visceral fat deposition. The combination of appetite reduction, decreased fat deposition and an improvement in the parameters associated with glucose intolerance makes a case for the use of exendin-4 as a treatment for diabetes. ANSWER 3 OF 8 MEDLINE ΑN 1999101946 MEDLINE DN 99101946 ΤI Repeated intracerebroventricular administration of glucagon-like peptide-1-(7-36) amide or exendin-(9-39) alters body weight in the rat. Meeran K; O'Shea D; Edwards C M; Turton M D; Heath M M; Gunn I; Abusnana ΑU S; Rossi M; Small C J; Goldstone A P; Taylor G M; Sunter D; Steere J; Choi S J; Ghatei M A; Bloom S R Imperial College School of Medicine Endocrine Unit, Hammersmith Hospital, London, United Kingdom. ENDOCRINOLOGY, (1999 Jan) 140 (1) 244-50. SO Journal code: EGZ. ISSN: 0013-7227. CY United States DTJournal; Article; (JOURNAL ARTICLE) LΑ English FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals EM 199903 EW 19990305 AΒ Central nervous system glucagon-like peptide-1-(7-36) amide (GLP-1)

19990305
AB Central nervous system glucagon-like peptide-1-(7-36) amide (GLP-1) administration has been reported to acutely reduce food intake in the rat. We here report that repeated intracerebroventricular (i.c.v.) injection of GLP-1 or the GLP-1 receptor antagonist, exendin-(9-39), affects food intake and body weight. Daily i.c.v. injection of 3 nmol GLP-1 to schedule-fed rats for 6 days caused a reduction in food intake and a decrease in body weight of 16 +/- 5 g (P < 0.02 compared with saline-injected controls). Daily i.c.v. administration of 30 nmol exendin-(9-39) to schedule-fed rats for 3 days caused an increase in food intake and

increased body weight by 7 + -2 g (P < 0.02 compared with saline-injected controls). Twice early i.c.v. injections of 30 nmor exendin-(9-39) with 2.4 nmol neuropeptide Y to ad libitum-fed rats for 8 days increased food intake and increased body weight by 28 +/- 4 g compared with 14 +/- 3 g in neuropeptide Y-injected controls (P < 0.02). There was no evidence of tachyphylaxis in response to i.c.v. GLP-1 or exendin-(9-39). GLP-1 may thus be involved in the regulation of body weight in the rat. ANSWER 4 OF 8 MEDLINE 1998010466 MEDLINE ΑN 98010466 DN Leptin interacts with glucagon-like peptide-1 neurons to reduce ΤI food intake and body weight in rodents. Goldstone A P; Mercer J G; Gunn I; Moar K M; Edwards C M; Rossi M; Howard J K; Rasheed S; Turton M D; Small C; Heath M M; O'Shea D; Steere J; Meeran K; Ghatei M A; Hoggard N; Bloom S R Department of Endocrinology and Metabolic Medicine, Imperial College School of Medicine, Hammersmith Hospital, London, UK. FEBS LETTERS, (1997 Sep 29) 415 (2) 134-8. Journal code: EUH ISSN: 0014-5793. Netherlands DTJournal; Article; (JOURNAL ARTICLE) LΑ English FS Priority Journals; Cancer Journals 199802 EMAΒ The adipose tissue hormone, leptin, and the neuropeptide glucagon-like peptide-1 (7-36) amide (GLP-1) both reduce food intake and body weight in rodents. Using dual in situ hybridization, long isoform leptin receptor (OB-Rb) was localized to GLP-1 neurons originating in the nucleus of the solitary tract. ICV injection οf the specific GLP-1 receptor antagonist, exendin(9-39), at the onset of dark phase, did not affect feeding in saline pre-treated controls, but blocked the reduction in food intake and body weight of leptin pre-treated rats. These findings suggest that GLP-1 neurons are a potential target for leptin in its control of feeding. L5 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2000 BIOSIS ΑN 2000:339764 BIOSIS DN PREV200000339764 Peripheral versus central effects of glucagon-like peptide-1 receptor agonists on satiety and body weight loss in Zucker obese rats. AU Rodriquez de Fonseca, Fernando; Navarro, Miguel; Alvarez, Elvira; Isabel; Chowen, Julie A.; Maestre, Olivia; Gomez, Raquel; Munoz, Raul M.; Eng, John; Blazquez, Enrique (1) (1) Departamento de Bioquimica y Biologia Molecular, Facultad de Universidad Complutense de Madrid, 28040, Madrid Spain Metabolism Clinical and Experimental, (June, 2000) Vol. 49, No. 6, pp. 709-717. print. ISSN: 0026-0495. DT Article English SL English The present study explores the potential utility of peripheral versus central administration of glucagon-like peptide-1 (GLP-1) receptor agonists in the regulation of feeding behavior in Wistar and Zucker obese rats. Acute central (intracerebroventricular (ICV)) and peripheral (subcutaneous (SC)) administration of both GLP-1 (7-36) amide and

exendin-4 resulted in a reduction in food

intake for at least 4 hours, exendin-4 being much fore potent than GLP-1 (7-36) amide especially after peripheral administration. Both Zucker obese rats (fa/fa) and their lean littermates (Fa/-) responded to acute central and peripheral administration of exendin-4. Moreover, in situ hybridization revealed specific labeling for the mRNA for GLP-1 receptors in several brain areas of both the obese and lean rats. The presence of this receptor was also detected by affinity cross-linking assays. Long-term SC administration of exendin-4 (1 single injection per day, 1 hour prior to the onset of the dark phase of the cycle) decreased daily food intake and practically blocked weight gain in obese rats. In contrast to previous studies, these findings show that peripheral (SC) administration of both GLP-1 receptor agonists also induces satiety and weight loss in rats, and suggest the potential usefulness of exendin-4 as a therapeutic tool for the treatment of diabetes and/or obesity.

- L5 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2000 BIOSIS
- AN 1999:74785 BIOSIS
- DN PREV199900074785
- TI Repeated intracerebroventricular administration of glucagon-like peptide-1-(7-36) amide or exendin-(9-39) alters body weight in the rat.
- AU Meeran, Karim; O'Shea, Donal; Edwards, C. Mark B.; Turton, Mandy D.; Heath, Melanie M.; Gunn, Irene; Abusnana, Salahedeen; Rossi, Michela; Small, Caroline J.; Goldstone, Anthony P.; Taylor, Gillian M.; Sunter, David; Steere, Joanna; Choi, Sang Jeon; Ghatei, Mohammad A.; Bloom, Stephen R.
- CS ICSM Endocrine Unit, Hammersmith Hosp., Du Cane Road, London W12 OHS UK
- SO Endocrinology, (Jan., 1999) Vol. 140, No. 1, pp. 244-250. ISSN: 0013-7227.
- DT Article
- LA English

icv

AB Central nervous system glucagon-like peptide-1-(7-36) amide (GLP-1) administration has been reported to acutely **reduce food**intake in the rat. We here report that repeated
intracerebroventricular (icv) injection of GLP-1 or the GLP-1 receptor antagonist, exendin-(9-39), affects food intake and body weight. Daily

injection of 3 nmol GLP-1 to schedule-fed rats for 6 days caused a reduction in food intake and a decrease in body weight of 16 +- 5 g (P < 0.02 compared with saline-injected controls). Daily icv administration of 30 nmol exendin-(9-39) to schedule-fed rats for 3 days caused an increase in food intake and increased body weight by 7 +- 2 g (P < 0.02 compared with saline-injected controls). Twice daily icv injections of 30 nmol exendin-(9-39) with 2.4 nmol neuropeptide Y to ad libitum-fed rats for 8 days increased food intake and increased body weight by 28 +- 4 g compared with 144 +- 3 g in neuropeptide Y-injected controls (P < 0.02). There was no evidence of tachyphylaxis in response to icv GLP-1 or exendin-(9-39). GLP-1 may thus be involved in the regulation of body weight in the rat.

- L5 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2000 BIOSIS
- AN 1998:425099 BIOSIS
- DN PREV199800425099
- TI Central and peripheral administration of Exendin-4 reduces food intake in rats.
- AU Bhavsar, S. P.; Watskins, J. J.; Young, A. A.
- CS Amylin Pharm. Inc., 9373 Towne Centre Dr., San Diego, CA 92121 USA
- SO Diabetologia, (Aug., 1998) Vol. 41, No. SUPPL. 1, pp. A214.

 Meeting Info.: 34th Annual Meeting of the European Association for the Study of Diabetes Barcelona, Spain September 11, 1998 European

for the Study of Diabetes . ISSN: 0012-186X.

DT Conference

LA English

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ANSWER 8 OF 8 BLOSIS COPYRIGHT 2000 BIOSIS
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      1997:504996 BIG
  AN
      PREV199799804199
  DN
      Leptin interacts with glucagon-like peptide-1 neurons to reduce
  TI
       food intake and body weight in rodents.
       Goldstone, Anthony P.; Mercer, Julian G.; Gunn, Irene; Moar, Kim M.;
  ΑU
      Edwards, C. Mark B.; Rossi, Michela; Howard, Jane K.; Rasheed, Shahnawaz;
      Turton, Mandy D.; Small, Caroline; Heath, Melanie M.; O'Shea, Donal;
       Steere, Joanna; Meeran, Karim; Ghatei, Mohammed A.; Hoggard, Nigel;
       Stephen R. (1)
       (1) Dep. Endocrinol. Metabolic Med., Imperial Coll. Sch. Med.,
  CS
  Hammersmith
       Hosp., Du Cane Rd., London W12 ONN UK
       FEBS Letters, (1997) Vol. 415, No. 2, pp. 134-138.
  SO
       ISSN: 0014-5793.
      Article
  DT
      English
  LΑ
      The adipose tissue hormone, leptin, and the neuropeptide glucagon-like
  AB
       peptide-1 (7-36) amide (GLP-1) both reduce food
       intake and body weight in rodents. Using dual in situ
       hybridization, long isoform leptin receptor (OB-Rb) was localized to
  GLP-1
       neurons originating in the nucleus of the solitary tract. ICV injection
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       the specific GLP-1 receptor antagonist, exendin(9-39), at the onset of
       dark phase, did not affect feeding in saline pre-treated controls, but
       blocked the reduction in food intake and
       body weight of leptin pre-treated rats. These findings suggest that GLP-1
       neurons are a potential target for leptin in its control of feeding.
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  L3
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       2000
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